Training in Methods in Computational Neuroscience

Marine Biological Laboratory
Woods Hole, MA

August 2 - August 29, 1992

James M. Bower and Christof Koch, Directors

Course Report

Summary of 1992

The 1992 final version of this course with Bower and Koch as Directors enrolled a total of 23 students including two post-doctoral fellows, one neurologist and one tenured faculty member. Other members of our ``team'' included five teaching assistants (TA; David Berkowitz, David Beeman, Öjvind Bernander, Dieter Jaeger and Maurice Lee) as well as the services of two computer managers (John Uhley and Maneesh Sahani) for setting up and maintaining all 28 workstations. Finally, William (Bill) Bialek spent one month with us at the MBL and was extremely helpful to us (in terms of teaching 3 classes) as well as interacting substantially and continuously with the students.

We felt (and the students appear to agree) that this year was the high point of the courses we organized and taught over the previous five years (starting from scratch in 1988). Different from last year, we experienced no significant problems with the weather (i.e. no hurricane), with students, with our simulator software or with the lecturers.

Lectures

The course went very well in terms of the lectures. After four years of experimenting with speakers and topics, we converged onto a set of competent, relevant and lively speakers. This core group of faculty includes in order of appearance: Paul Adams, Idan Segev, Nancy Kopell, Avis Cohen, Eve Marder, John Rinzel, Bill Baird, Joe Atick, Richard Andersen and Rodney Douglas. The response of the students to these faculty was uniformly high: this group of faculty managed to capture the imagination of the students. In previous years, a common complaint was that some fraction of the faculty spent most of their lectures on their individual research topics, rather than focusing more broadly on methodological or on conceptual issues (the trade-off between depth versus breath). This core group spent most of their three to five lectures which they each gave (including one or more tutorials) on general issues, and, between them, spanned the themes relevant to "Computational Neuroscience", from single neurons to chips, neural networks and information processing. This group should certainly be considered for any future course.

We continued our informal "refreshment" hour, where students could spend time with the faculty on Tuesday and Thursday evenings. Students appreciated meeting the lecturers on this informal basis. We also continued our practice of establishing small working groups of students interested in similar types of modeling problems. We had

three such groups (focused on "Vision" (CK), "CPG's" (JB) and "Oscillations and Synchronization" (CK) and met throughout the course to share problems and solutions. This was particularly valuable with respect to the student projects in the student lab. We increased the number of tutorials devoted to more formal, mathematical topics compared to last year ("Linear algebra" taught by Ken Miller; "Information Theory" taught by Joe Atick; "Probability Theory" taught by Bill Bialek; "Phase-Space Analysis I and II" taught by John Rinzel and Nancy Kopell) but also continued with the tutorials devoted to more practical issues, such as the working of NEURON or GENESIS, the details of the Hodgkin-Huxley model and numerical methods for solving differential equations. Different from the previous four years, where the level of interaction between students and faculty (as expressed by the students themselves) was high during the first three weeks of the course but diminished greatly during the last week (because the faculty spent most of their time attending T. Sejnowski's "Computational Neuroscience Workshop"), student-faculty interaction was also high in the last week due to the conscious choice of both directors to participate only minimally in Sejnowski's workshop.

We again managed to achieve a relatively high female-to-male ratio (7 out of 23 students), which is quite unusual for a theoretical field. Given that we also had a significant number of female faculty (e.g. Kopell, Cohen, Marder), this had a significant positive impact on the course atmosphere.

Computer Managers and Teaching Assistants

We had one full-time system manager (from Caltech) present at almost all times of the day (and the night) for the duration of the course. Furthermore, John Uhley, our hardware/software consultant at Caltech, set up all 28 workstations (a combination of IPC's and SPARCstations from SUN Microsystems). We therefore could assure that each of the 23 students had a continuously working and fully networked state-of-the-art workstation available throughout the duration of the course.

We had a total of 5 teaching assistants available to help all students. At least one TA was present from noon until midnight in the computer lab to answer questions. In particular, David Berkovitz (a MD from Yale University who is in his 3rd year of his PhD in Neuroscience) deserves much praise for his non-stop commitment towards the students of the course far and beyond the call of duty! We had on TA (Öjvind Bernander from Caltech) who was responsible for the single-cell simulator NEURON, while the other three TA's (David Beeman, Dieter Jaeger and Maurice Lee) were responsible for all GENESIS related questions and projects.

Laboratory/Simulators

Given last year's criticism from many students that we should also make the single-cell simulator NEURON (written by Mike Hines) available to them, we did this year and were surprised by the low use of this very convenient software package. Only two students used NEURON for their projects. All other students continued to use GENESIS, developed by one of us (JB) at Caltech. One reason for this

choice is the large amount of documentation and previously written software available for GENESIS. Furthermore, NEURON does not lend itself easily to simulating more than one neuron.

In order to provide students with additional time to finish their computer simulation projects, we decided to add an optional fifth week following the four week long course, giving students the opportunity to finish their projects on the machines while help was still around. However, only one student took advantage of this opportunity.

Enrollment Information 1992:

There were 37 applicants in 1992. Twenty three students were accepted including 2 who are full-time faculty members. All students who were offered a place in the class accepted. The class of 23 had 1 undergraduate, 18 graduate students 2 postdoctoral and 2 faculty. Of this class there were 16 males and 7 females. **Appendix A** shows the enrolled students. Student projects are summarized in **Appendix E.**

1992 Faculty.

A list of faculty from 1992 is shown in **Appendix B** and the 1992 lecture schedule is in **Appendix C.**

Administrative Matters

Advertising and Admissions:

The MBL course announcement is sent to several thousand departments and individuals for posting. Advertisements are placed in *Science, Nature* and *Cell.* In addition, announcements have appeared in the *Newsletter, Society for Neuroscience* and *Neural Computation,* and on several electronic bulletin boards. A mailing of course announcements and minority opportunities at the MBL is sent to an extensive mailing list of minority institutions and contacts provided by the American Society of Microbiology as well as a list of minority graduate students provided by the American Physiological Society. **Appendix D** has examples of advertising material.

Other Support:

Support for this training program was obtained from the NIMH, McDonnell-Pew Program in Cognitive Neuroscience and the Office of Naval Research, as well as hundreds of thousands of dollars worth of workstations from Sun Microsystems.

Changes in Course Directorship

A search committee led by Dr. Terry Sejnowski recommended Drs. David Tank and David Kleinfeld of Bell Labs as the new course directors for 1993 -1997. They have accepted this task and are the new leaders. Their plan appears directly below.

Plans for 1993

This training program is intended as an intensive survey of issues and methods in computational neuroscience. The course covers a variety of topics in the study of how biophysical and biochemical properties of neurons and synapses, together with the architecture of neural circuits, produce animal behavior. The range of topics includes cellular and synaptic properties, the dynamics of small networks, the concepts of the receptive field and information flow and processing in nervous systems. The effectiveness of models, at both the detailed realistic level and at the abstract level, are thoroughly discussed within the context of these topics. Our goal for the program is twofold. First, to provide students with the ability to formulate focused, pertinent questions in computational neuroscience. Second, to provide them with a knowledge of tools to attack these questions.

The course includes both a lecture series and a computer laboratory in which students gain hands-on experience with proven simulation techniques. The lectures are given by invited faculty whose work represents the highest levels of achievement in computational neuroscience. Relevant reprints of scientific articles will be available to the students, and the discussion of these papers may be an integral part of the lectures. As a further guide for the students, some of the material has appeared in the book "Methods in Neuronal Modeling: From Synapses to Networks (by C. Koch and I. Segev, editors, MIT Press, 1989).

Lectures 1993

Students attend lectures six mornings and five evenings a week. Each lecture consists of a ninety minute presentation by a faculty member followed by an extended discussion. For all of our topics, we plan to have lectures on the experimental evidence nominally followed by lectures on models. In some cases complimentary approaches toward modeling will be presented. The discussion period will allow students to query all of the lectures on a given topic, and thus formulate their own conclusions on the success or failure of different approaches.

1. Basic Cellular & Synaptic Physiology

The first part of the course is largely devoted to presenting and discussing basics experimental facts about cellular physiology and synaptic dynamics and mathematical models of single neurons and synapses. The lecture sequence is:

David Kleinfeld

Basic electrochemistry pertinent to physiology, including diffusion, equilibrium potentials, permeability and relevant thermodynamic relations.

David Tank

The notion of voltage -gated conductance and nonlinearities in membranes. The key experimental results of Hodgkin and Huxley and basic aspects of the Hodgkin-Huxley model.

David Tank
Basic synaptic physiology, including the dependence of release on voltage and Ca2+.

Idan Segev
Introduction to cable theory; Rall model and compartmental models.

Artie Sherman
Review of numerical methods used in compartmental model simulations. Integrating stiff differential equations.

David Tank
Calcium diffusion, pumping, buffering. Models of calcium dynamics in cell bodies, dendrites, and synaptic terminals.

John Rinzel
More advanced topics in Hodgkin-Huxley models: thresholds for action potential firing, firing rates, rebound excitation.

John Rinzel
Reduced models of single cell dynamics and phase plane analysis.

David McCormick
Ionic currents in thalamic and cortical cells.

David McCormick
Detailed models and simulations of the electrical properties of thalamic and cortical neurons.

John Rinzel
Reduced models of bursting neurons.

2. Nervous System Development & Plasticity
The second part of the course is devoted to presenting and discussing experimental facts about development and plasticity in the nervous system and mathematical models of these phenomena. The lecture sequence is:

David Van Essen
Synaptic plasticity and development of synaptic junctions; experimental evidence and models.

David Tank
Short term synaptic enhancement, phenomenological models, calcium dynamics and synaptic transmission.

Bruce McNaughton
Long Term Potentiation (LTP) - experimental facts and mathematical and computer models.

John Lisman
Models of the biochemical cascade underlying LTP induction; molecular switches; chemical computation.

Bill Bialek
A review of linear algebra relevant to models of cortical map development.

Michael Stryker
Cortical maps and development in primary visual areas.

Ken Miller
Mathematical models of cortical map formation.

3. Small Networks
These lectures concern systems with a small number of cells and synapses, with emphasis on invertebrate systems. The lecture sequence is:

Eve Marder
Overview of rhythmic pattern generators that govern breathing, digestion and locomotion in a variety of invertebrates. The diversity of mechanisms found in biology to "solve" similar problems will be emphasized.

Bard Ermentrout
Review of dynamical systems, with an emphasis on systems with two and three degrees of freedom. The emphasis is on approximate, analytic techniques.

Karen Sigvardt
The experimental evidence on pattern generation within the spinal cord of lamprey. Emphasis on the cellular basis of the rhythm and variations in the pattern for different behaviors.

Nancy Kopell
Models of coupled oscillators that mimic variations in the pattern of rhythmic motion observed in lamprey. A comparison of the data with predictions of these reduced models.

William Frost
The underlying cellular and synaptic physiology for the circuit that generates the escape swim response in Tritonia.

David Kleinfeld
Associative network approach toward modeling rhythmic pattern

generating with emphasis on the swim response in Tritonia.

Roger Traub
Models with realistic neurons, with an emphasis on large-scale modeling of epileptic phenomena in hippocampus.

Rodolpho Llinas
The interaction between cellular properties and the dynamics of networks. The emphasis is on the cerebellar-olivary loop.

4. Cortical Processing
This series of lectures focuses on processing in cortical areas. The notion of receptive fields is introduced and debated in light of a large body of evidence from visual and other regions. The concepts of local versus global processing are emphasized.

Rodney Douglas
A review of cortical anatomy, with an emphasis on thalamic - cortical projections, functional specialization of different cortical areas and the anatomical and physiological classes of neurons observed in cortex.

Christof Koch
An overview of algorithms, primarily from computer vision, that allow global features of the visual field to be identified. The prediction from these algorithms for the architecture of neuronal systems will be emphasized.

Stephen Kosslyn
The experimental evidence for the involvement of multiple cortical areas in sensory tasks and mental imagery. These lectures will illustrate that the response of neurons may depend on activity beyond that of their immediate neighbors.

John Maunsell
The notion of the classic receptive field with an emphasis on the visual system. The mapping of features across multiple areas of
cortex and the functional relationship between neurons that comprise different maps is discussed.

Terrence Sejnowski
Connectionist models of receptive fields, with an emphasis on visual cortex. This lecture will describe how the response of many neurons do not have a low complexity description.

John Maunsell
The notion of the receptive field is reanalyzed in light of global stimuli, such as illusionary contours, that modulate the firing properties of neurons.

Haim Sompolinsky

Models that address how the interactions between cortical neurons can control or modulate the receptive fields of these cells.

Charles Gray
The role of temporal dynamics in cortical processing. Experimental evidence from motor and visual areas, with an emphasis on modulation of synchronize by global features in the stimuli.

David Kleinfeld
Models for synchronizing interactions between neurons and groups of neurons. The emphasis is on temporal dynamics in the visual system.

5. Coding and Internal Representation
This series of lectures examines how information in the nervous system is represented, either in terms of local codes or population codes. Theories of coding and their relation to experimental evidence from a variety of systems are discussed. The lectures include:

John Hopfield
The representation of memories within associative networks is reviewed, along with the dynamic properties of such networks and appropriate learning algorithms.

Apostolos P. Georgopoulos
The experimental results for population coding in motor cortex for movement are presented, along with the effect of memory and mental imagery on the underlying neuronal activity.

William Bialek
Review of information theory, with an emphasis on measures that are valuable for characterizing sensory inputs and neuronal responses.

Joseph Attick
An introduction to Barlow's principle of decorrelation and the analysis of coding of visual information in the retina according to this principle. The interplay between models and the experimental evidence is emphasized.

William Bialek
A brief overview of visual processing in the fly, with a discussion of models for the coding of visual motion by the firing rate of neurons. This lecture will also introduce the concept of optimal filtering.

Sebastian Seung
The theory of population codes and the application of the theory to experimental evidence (e.g., the work of Georgopoulos). Optimal choices for discrimination tasks will be discussed within the content of maximum likelihood.

The computer laboratory is composed of a large number of state-of-the-art graphics workstations. In 1993 we will need to rent SUN SPARCstations through an outside vendor. This arrangement may be supplemented by workstations loaned through a special arrangement with Sun Microsystems, Incorporated.
The use of workstations assures that the most recent state of the art equipment is available for the students to use. In the rapidly evolving technology of graphics workstations, this is a major advantage. We expect to have a workstation for every student. The workstations are part of a LAN connected to the MBL ethernet.

Faculty Affiliations 1993

Course Directors
DAVID KLEINFELD, AT&T Bell Laboratories, Murray Hill, NJ
DAVID W. TANK, AT&T Bell Laboratories, Murray Hill, NJ

Faculty
JOSEPH ATICK, Rockefeller University, New York, NY
WILLIAM BIALEK, NEC Research Institute, Princeton, NJ
EMILIO BIZZI, Massachusetts Institute of Technology, Cambridge, MA
RODNEY JAMES DOUGLAS, MRC Anatomical Neuropharmacology Unit, Oxford, England
BARD ERMENTROUT, University of Pittsburgh, Pittsburgh, PA
WILLIAM N. FROST, University of Texas Medical School, Houston, TX
APOSTOLOS P. GEORGOPOULOS, VA Medical Center, Minneapolis, MN
CHARLES GRAY, The Salk Institute, La Jolla, CA
MICHAEL HINES, Duke University Medical Center, Durham, NC
JOHN J. HOPFIELD, California Institute of Technology, Pasadena, CA
RODERICK JENSEN, Texas A&M University, College Station, TX
CHRISTOF KOCH, California Institute of Technology, Pasadena, CA
NANCY KOPELL, Boston University, Boston, MA
STEPHEN M. KOSSLYN, Harvard University, Cambridge, MA
JOHN E. LISMAN, Brandeis University, Waltham, MA
KARL L. MAGLEBY, University of Miami School of Medicine, Miami, FL
EVE E. MARDER, Brandeis University, Waltham, MA
JOHN H.R. MAUNSELL, University of Rochester, Rochester, NY
DAVID A. McCORMICH, Yale University School of Medicine, New Haven, CT
BRUCE L. McNAUGHTON, University of Arizona, Tucson, AZ
KENNETH D. MILLER, California Institute of Technology, Pasadena, CA
JOHN RINZEL, National Institutes of Health, Bethesda, MD
DAVID A. ROBINSON, Johns Hopkins University, Baltimore, MD
IDAN SEGEV, Hebrew University, Israel
TERRENCE J. SEJNOWSKI, The Salk Institute, San Diego, CA
ARTHUR SHERMAN, National Institutes of Health, Bethesda, MD
KAREN SIGVARDT, University of California @ Davis VA Medical Center, Martinez, CA
MICHAEL STRYKER, University of California Medical Center, San Francisco, CA
ROGER TRAUB, IBM T.J. Watson Research Center, Yorktown Heights, NY
DAVID VAN ESSEN, Washington University Medical School, St. Louis, MO
P. WALLEN, Iii Karolinska Institute, Sweden

Laboratories 1993

The objective of the laboratory part of the course is to advance the students analytical and numerical simulation skills in modeling specific aspects of nervous systems. We will not feature any single piece of simulation software. Rather, we will

have a set of laboratory-related lectures and on-site TA's for each of several packages. For single neuron and neural network simulations, we will have the packages GENESIS (from J. Bower's lab at Caltech) and NEURON (from Michael Hines at Duke). For general purpose dynamical systems analysis we will have DSTOOL (from John Guckenheimer at Cornell) and PHASELINE (from Bard Ermentrout at U. Pittsburgh). In addition, the general mathematical analysis package MATHEMATICA (Wolfram Research, Inc) and the interactive graphics package IDL (Research Systems, Inc.) will be available.

Appendix A. Students with Project Title, 1992

ERIK COOK, Graduate Student, Neuroscience, Baylor University, Houston, TX
Course Project: Effects of Inhibition on Pyramidal Cell Model

ADELLE COSTER,Graduate Student, Electrical Engineering, University of New South Wales, Australia
Course Project: Energy Minimization in Neural Networks

SHARON CROOK, Graduate Student, Mathematics, University of Maryland, College Park, MD
Course Project: Mathematical Model of Central Pattern Generator

WINRICH FREIWALD, Graduate Student, Biology, Tubingen University, Germany
Course Project: Modelling Canonical Microcircuit Activitypatterns of the Neocortex

ALBERTO HERRERA-BECERRA, Graduate Student, Electrical Engineering, University of Mexico, Mexico
Course Project: Study of the Dynamical Behaviours Associated with Degenerate Hopf Bifurcations in the Hodkin and Huxley Model.

MARTIN HUBER,Graduate Student, Physiology, Phillips -University-Marburg, Germany
Course Project: Electical Coupling Between Endogenous Bursting Neurons in Small Networks.

MICHAEL IRIZARRY, Medical Resident, Neurology, Massachusetts General Hospital, MA
Course Project: Membrane Properties of a Neostriatal Neuron and Dopamine Modulation

RANU JUNG, Postdoctoral Fellow, Cardiology, Case Western Reserve University, OH
Course Project: Leech Heart half-oscillator

BRANDT KEHOE, Faculty, Physics, California State University, Fresno, CA
Course Project: Interspike Interval Distributions Generated by Model Neurons

ILAN LAMPL, Graduate Student, Neurobiology, Hebrew University, Israel
Course Project: Oscillatory Activity of Inferior Olive Neurons

MITCHELL MALTENFORT, Graduate Student, Biomedical Engineering, Northwestern University, Chicago, IL
Course Project: A Model Motoneuron and Renshaw Cell

FERENCE MECHLER, Graduate Student, Neural Science, New York University, New York City, NY
Course Project: Cortical Simple Cells in Area 17 of the Cat

JILL NICOLAUS, Graduate Student, Organismal Biology and Anatomy, University of Chicago, IL
Course Project: Network Models of Inhibition in Turtle Visual Cortex

HARMON NINE, Graduate Student, Computational Neuroscience, University of Michigan, Ann Arbor, MI
Course Project: NMDA Receptors: Origins and Mechaninsms of Post-synaptic Potentials

MONICA PAOLINI, Graduate Student, Cognitive Science, University of California, San Diego, CA
Course Project: Poggio Model of the Optical Flow

YIFAT PRUT, Graduate Student, Physiology, Hebrew University, Israel
Course Project: The Single Cell as a Coincidence Detector

IRIS REUVENI, Graduate Student, Physiology, Ben Gurion University of the Negev, Israel
Course Project: The Role of Inhibition in Input Output Relation in Sparse Network

EMILIO SALINAS, Graduate Student, Biophysics. National University, Mexico
Course Project: Simulation of the AB-PD Two-cell Network in the Stomatogastric Ganglion of the Lobster

EYAL SEIDEMANN, Graduate Student, Biophysics, Tel Aviv University, Israel
Course project: Models of Attracter Neurons Networks Operating in Low Spike Rate

NANGIAVARAM SEKAR, Graduate Student, Neuroscience, University of Iowa, Iowa City
Couse Projects: A Feedback Based Model of Synaptic Plasticity.

MICAH SIEGEL, Undergraduate, Electrical Engineering, Yale University, CT
Course Project: Phase-sychronization in the Oscillatory Activity of Coupled Networks

MARK TOMMERDAHL, Faculty, Physiology, University of North Carolina, Chapel Hill, NC
Course Project: NMDA Receptor Effect on Neuron Responsivity at Low Velocities

YI-XIONG ZHOU, Graduate Student, Ophthalmology, McGill Vision Research Center, Canada
Course Project: Spatial Freqeuncy Properties of the Primary Visual Cortical Neurons

Appendix B. Faculty and Assistants. 1992

Directors

JAMES BOWER, California Institute of Technology, Pasadena, CA
CHRISTOF KOCH, California Institute of Technology, Pasadena, CA

Faculty

PAUL R. ADAMS, Howard Hughes Medical Institute, Stony Brook, NY

RICHARD ANDERSEN, Massachusetts Institute of Technology, Cambridge, MA

JOSEPH J. ATICK, Rockefeller University, New York, NY

WILLIAM BIALEK, NEC Research Institute, Princeton, NJ

AVIS COHEN, University of Maryland, College Park, MD

RODNEY JAMES DOUGLAS, MRC Anatomical Neuropharmacology Unit, Oxford, England

NANCY KOPELL, Boston University, Boston, MA

RODOLPH R. LLINAS , New York University Medical Center, New York, NY

EVE MARDER, Brandeis University, Waltham, MA

MICHAEL V. MASCAGNI, Supercomputing Research Center, Bowie, MD

KENNETH D. MILLER, California Institute of Technology, Pasadena, CA

JOHN RINZEL, National Institutes of Health, Bethesda, MD

IDAN SEGEV, Hebrew University, Israel

TERRENCE SEJNOWSKI The Salk Institute, San Deigo, CA

Teaching Assistants

DAVID BEEMAN, University of Colorado, Boulder, CO
DAVID BERKOWICZ, Yale University Medical School, New Haven, CT
OJVIND BERNANDER, California Institute of Technology, Pasadena, CT
DIETER JAEGER, California Institute of Technology, Pasadena, CA
MAURICE LEE, California Institute of Technology, Pasadena, CA

Computer Managers

MANEESH SAHANI, California Institute of Technology, Pasadena, CA
JOHN UHLEY, California Institute of Technology, Pasadena, CA

Appendix C. Schedule of Lectures and Tutorials, 1992

Sunday, August 2
James Bower/Christof Koch
Introduction to the course

Monday, August 3
James Bower
Introduction to the course
Idan Segev
Introduction to cable theory
Paul Adams
Voltage- and agonist-dependent ionic channels
TUTORIAL: John Uhley
Introduction to workstations, UNIX and X windows

Tuesday, August 4
Paul Adams
Hodgkin-Huxley nerve equations
Idan Segev
Compartmental models of neurons
TUTORIAL: Maurice Lee
Single cell and neural network simulator: GENESIS

Wednesday, August 5
Michael Mascagni
Solving ordinary differential equations
Christof Koch
Synaptic input; nonlinear interaction between synaptic inputs
TUTORIAL: Michael Mascagni
Ordinary differential equations

Thursday, August 6
Paul Adams
Potassium and calcium-dependent currents;
bullfrog sympathetic ganglion
Idan Segev
Electrical models of dendritic spines
Michael Mascagni
Solving Partial differential equations

Friday, August 7
Paul Adams / Christof Koch
Voltage-dependent NMDA synaptic receptors
Christof Koch
Calcium diffusion; calcium dynamics and dendritic spines

TUTORIAL: Michael Mascagni
Simulating neurons and networks on parallel computers

Monday, August 10
Christof Koch
Stochastic models of nerve cells; integrate-and-fire neurons
Rudolfo Llinas
Calcium dynamics in Purkinje cells
Rudolfo Llinas
The function of the thalamus

Tuesday, August 11
Joe Atick
Introduction to information theoretical approaches in neuroscience
TUTORIAL: Ken Miller
Linear systems analysis, eigenvectors and eigenvalues

Wednesday, August 12
Joe Atick
Redundancy reduction and retinal coding
Ken Miller
Introduction to neural development
TUTORIAL: Joe Atick
Information theory

Thursday, August 13
Ken Miller
Development in the visual system: orientation tuning and ocular dominance
Charles Stevens
Long-Term Potentiation (LTP) I
TUTORIAL: Joe Atick / Ken Miller
Probability theory

Friday, August 14
Charles Stevens
LTP II
Bill Bialek
Computation in the fly's visual system

Monday, August 17
Bill Bialek
Analysis of information transfer in the fly's visual system
John Rinzel
Phase-space analysis of Hodgkin-Huxley like systems;
theory of dynamical systems
TUTORIAL: Bill Bialek

Probability, Information, and Neural Coding

Tuesday, August 18
Avis Cohen
Single cell oscillators in vertebrates;
John Rinzel
Synaptic vs. electrical coupling of spiking cells
TUTORIAL: John Rinzel
Phase-space analysis for non-bursting and bursting cells

Wednesday, August 19
Nancy Kopell
Phase-space analysis of the lamprey network
Eve Marder
Central Pattern Generators Networks
TUTORIAL: Nancy Kopell
Phase-space analysis for coupled cells

Thursday, August 20
Eve Marder
Modeling Central Pattern Generators
Tony Zador
Linking single hippocampal cells to associative memory

Friday, August 21
James Bower
Associative learning in olfactory cortex
Christof Koch
The correlation model of motion detection

Sunday, August 23. until Friday, August 28.
Computational Neuroscience Workshop,
organized by Terrence Sejnowski

Monday, August 24
Richard Andersen
The primate visual system: an overview
Rodney Douglas
The basic cells types in mammalian cortex: anatomy,
distribution and physiology
TUTORIAL: Rodney Douglas
Modeling neurons in silicon

1992 Schedule.

Tuesday, August 25
James Bower
  40 Hz oscillations: experimental findings in visual and olfactory cortex
Christof Koch
  Oscillations and synchronization: an overview of models

Wednesday, August 26
Terry Sejnowski
  Dynamical models of eye movements

Thursday, August 27
Terry Sejnwoski
  Understanding cortical computations using back-propagation
Richard Andersen
  Physiological and neuronal network approaches to study
  extrastriate cortical areas involved in spatial perception

Friday, August 28
Rodney Douglas
  The canonical microcircuit of cortex
Presentations of Student Projects to the MBL Community

Methods in COMPUTATIONAL NEUROSCIENCE

August 3 - August 31, 1993

This is an intensive, four week lecture/laboratory course that addresses issues relevant to computational neuroscience: the study of how the biophysical and biochemical properties of neurons and synapses, together with the architecture of neural circuits, produce animal behavior. The course is designed to teach students to formulate questions about computational aspects of a nervous system, to provide the analytical and numerical simulation tools necessary to answer those questions, and to allow students to interact with established investigators in this field.

The daily lectures provide a broad view of computational neuroscience, while at the same time discussing in detail the interplay between models and experiments for specific systems. One series of lectures focuses on the chemical and electrical dynamics of individual neurons and synapses. A second series addresses the use of exact models of single cells, versus reduced neuronal models, in the analysis of networks. A third series of lectures considers development of nervous systems. A final series addresses the detection, coding and processing of external stimuli within nervous systems, with an emphasis on cooperative phenomena. Reviews on areas of applied mathematics relevant to the above topics are also presented.

The laboratory section of the course provides students with a unique opportunity to advance their analytical and numerical simulation skills in modeling specific aspects of nervous systems through tutorial projects together with an individualized modeling project. Each student is supplied with a UNIX graphic-color workstation and state-of-the-art software designed for the analysis of both single-cell dynamics and large network properties. The packages include GENESIS and NEURON as well as DSTOOL and PHASEPLANE. In addition, the general mathematical analysis package MATHEMATICA® and the interactive graphics package IDL® are available.

The course is designed for advanced graduate students, postdoctoral fellows, and faculty members in a variety of disciplines, including neurobiology, physics, electrical engineering, computer science, and psychology. Familiarity with neurophysiology, basic mathematical skills, i.e., calculus, linear algebra and differential equations, and computer programming skills, is highly desirable. Admission in the course is limited to 23 students.

This program is funded in part by a training grant from NIMH, and grants from the Office of Naval Research and Pew Charitable Trusts.

Course Directors: David Kleinfeld, and David W. Tank, AT&T Bell Laboratories.

Faculty Joseph Atick, Rockefeller University; William Bialek, NEC Research Institute; Rodney James Douglas, MRC; Bard Ermentrout, University of Pittsburgh; William N. Frost, University of Texas Medical School; Apostolos P. Georgopoulos, VA Medical Center; Charles Gray, Salk Institute; John J. Hopfield, California Institute of Technology; Christof Koch, California Institute of Technology; Nancy Kopell, Boston University; Stephen M. Kosslyn, Harvard University; John E. Lisman, Brandeis University; Rodolfo R. Llinas, New York University Medical Center; Eve E. Marder, Brandeis University; John H.R. Maunsell, University of Rochester; David A. McCormick, Yale University School of Medicine; Bruce L. McNaughton, University of Arizona; Kenneth D. Miller, California Institute of Technology; John Rinzel, National Institutes of Health; David A. Robinson, Johns Hopkins University; Idan Segev, Hebrew University; Terrence J. Sejnowski, Salk Institute; H. Sebastian Seung, AT&T Bell Laboratories; Arthur Sherman, National Institutes of Health; Karen Sigvardt, University of California, Davis; Haim Sompolinsky, Hebrew University; Michael Stryker, University of California Medical Center; Roger Traub, IBM Corporation; and David Van Essen, Washington University Medical School.

Laboratory Instructors: David Berkowitz, Yale University Medical School; David Golomb, National Institutes of Health; Michael Hines, Duke University Medical Center; Roderick Jensen, Texas A&M University; Terrance Kovacs, AT&T Bell Laboratories; and Rafael Yuste, AT&T Bell Laboratories.

Applications are evaluated by an admissions committee. Notification of admissions decisions are mailed within two weeks of those decisions.

APPLICATION DEADLINE:
May 21, 1993

Tuition:
$1,500 (includes room and board)
Partial financial aid is available.

For further information and application forms, contact:

Dorianne Chrysler
Admissions Coordinator
Marine Biological Laboratory
Woods Hole, MA 02543, USA
(508) 548-3705, ext. 401.

MARINE • BIOLOGICAL • LABORATORY

Appendix E. Student Laboratory Reports, 1992
[These are largely undedited reports from the students]
Training in Methods in Computational Neuroscience
Marine Biological Laboratory, Woods Hole

ERIK COOK, Graduate Student, Neuroscience, Baylor University, Houston, TX
Course Project: Effects of Inhibition on Pyramidal Cell Model

Plan:

1) Convert some of my simulations from NEURON to GENESIS (and thus learn GENESIS).
2) Develop a realistic inhibtory model.
3) Further explore the effects of inhibition on my pyramidal cell model.
4) Further quantify how the dynamic range of a neuron affects it's ability to store patterns.

Accomplished:

The type of simulation I was interested in was one that would take a large compartmental model, randomly assigned synapses, and then run the model for 15ms and see if the model fired an action potential anytime during the 15ms. I then repeat this procedure hundreds of times based on a complex algorithm designed to evaluate the storage capacity of my realistic pyramidal cell model. Fast simulation times are obviously very important.

I only accomplished 90% of my first goal. I implemented simulations I had written for NEURON into Genesis, but did not have time to fully test these simulations. Converting my NEURON simulations to Genesis turned out to be a nontrivial task. The reason being that the Genesis hsolve object for efficiently solving large compartmental models was not integrated well with many other aspects of Genesis. This required a large amount of TA time as the TA's themselves could not get the hsolve to work properly with my model. I'm happy to report that eventually things got working. Eventually I will send Dave Beeman a short description of the Genesis hsolve scripts that did work and a detailed description of the things that don't work with the current version of hsolve (I'll send it probably after Sept. 10).

I did, however, learn many aspects of the Genesis source code and data structures that I would not have had everything worked. I now feel confident that I can continue to work with Genesis after completing this course.

I will finish my evaluation of my Genesis simulations sometime after Sept. 10 and will let you know how Genesis and NEURON compare for my particular application.

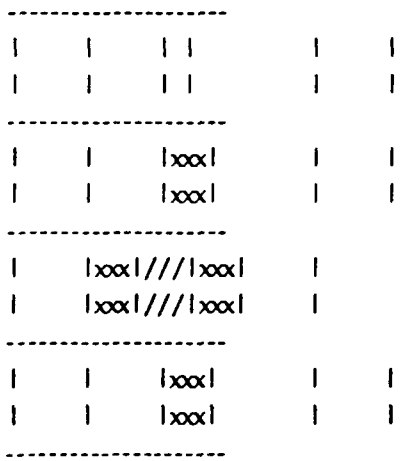
ADELLE COSTER,Graduate Student, Electrical Engineering, University of New South Wales, Australia
Course Project: Energy Minimization in Neural Networks

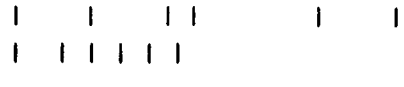
I came initially to the course with what I realise now were unrealistic expectations, but I think that GENESIS has been a good learning tool for me in that I now know about the depth of knowledge of specifics of a system one needs to know about in order to begin simulating. The work I ended up doing mainly revolved around the Squid2 tutorial system, I made a few minor parameter changes etc in the scripts - but nothing useful. I would like to see if I can get into writing some new objects for a network model of perhaps fairly simple neurons and then develop some system to explore various energy functions in the network. I think that this may be possible in the future as I think I now know enough to get a start. My project ended up being an exploration of the capabilities of GENESIS itself - for instance it is limited in terms of large networks (~5 or more cells start to be really slow). The single cell capabilities of the system are excellent however, and at some later stage I hope to exploit this. Due to my lack of knowlege of the specifics of neural systems I may not have got as much out of the simulation as some of the other students, however, I do feel that it has been a valuable learning tool for me, and that it is a very important part of the course. I have really enjoyed the course - it has been a great introduction for me into the realm of neuroscience. If I end up with any usable scripts at some later stage I will send them across.

SHARON CROOK, Graduate Student, Mathematics, University of Maryland, College Park, MD
Course Project: Mathematical Model of Central Pattern Generator
My project is a simulation of a central pattern generator which consists of four coupled oscillators. It is designed for flexibility with cell properties which vary with injection current. The connections may currently be set to either inhibitory or excitatory synaptic connections where the user may define the strength and delay of each connection. I also plan to implement an option for electrical coupling of cells.

There is a graphics window which shows the network architecture and allows the user to interactively select one of the cells in the network using the mouse. When a cell is selected, a graph for that cell appears along with a window which allows the user to change the parameters for the cell and any of its possible connections with the other cells in the network. When the simulation is run, the graphical representations of the cells change color where the color varies with the voltage.

WINRICH FREIWALD, Graduate Student, Biology, Tubingen University, Germany
Course Project: Modelling Canonical Microcircuit Activitypatterns of the Neocortex
A brief description of my project:
Recently rhre has been a lot of talk about the so called 40Hz-
oscillations in the activity of single neocortical cells and their field potentials. Interest in this phainomenon has arisen partly because it has been proposed that these oscillations have a function in "higher" behavioral tasks such as object-recognition or even awareness and consciousness, partly because this role has been doubted on the basis of similar activity-patterns in the piriform cortex. There do already exist various simulations confined to this topic. The more biologically realistic, though, lack a anatomical details of the neocortex.
My aim was to build a model of the neocortex, based on the canonical
microcircuit proposed by Douglas and Martin, and to study it`s activitypatterns. Especially I wanted to see, whether such a basic model exhibits this kind of oscillatory activity. The second step after replication of experimental findings is to make predictions for future experiments.
My GENESIS-Program consists of 25 triplets of multicompartmental cells, placed on the surface of a torus, each triplet receiving random input. The torus can be thought of as the "cortex", the random input sources as "thalamic input".
The three cells constituting the triplet are two five-compartmental pyramidal cells and a one-compartmental inhibitory interneuron. These all have active Hodgkin-Huxley-like sodium- and potassium-channels, excitatory and inhibitory synapses. These cells and there connections are to represent the basic properties of Douglas` and Martin`s circuit. These triplets are placed on a 5*5-grid, and the pyramidal cells are connected to their neighbour counterparts in a von-Neumann-like enviroment (position /// to positions xxx):





In order to account for margin-problems these were put together so to build a torus. On it's surface the interconnected triplets are placed. The analysis was performed with auto- and croosscorrelograms; I also analyzed a model consisting only of pyramidal cells and excitatory connectoins, each cell receiving random input.

The activity of 25 pyramidal cells over a few seconds was greaphically displayed.

The analysis of the models has just started. An interesting aspect of the behaviour of the simpel model is the wavelike occurrence and disappearence of activity in a large and variabel subset of the cells. The cells in the more complex model are sometimes synchronized, but mostly not.

[The simulation uses a modified genesis with Dieter's datanal library]

future plans:

- putting the cells into Neurokit-voltage-clamp-exoeriments to make them more realistic
- writing the cells to seperate files to make the auto- and cross-correlograms from more data
- making phaseplots of some cells to see, whether they show some kind of limit cycle behaviour
- improving the single cell anatomy the connection patterns

useful functions may be found in ../winrich/final/

ALBERTO HERRERA-BECERRA, Graduate Student, Electrical Engineering, University of Mexico, Mexico

Course Project: Study of the Dynamical Behaviours Associated with Degenerate Hopf Bifurcations in the Hodkin and Huxley Model.

Introduction:

J. Rinzel, Hassard and others had shown that the Hodgin & Huxley model presents a double Hopf Bifurcation taking the injection current as the free parameter of the system. Their results mean that the H&H model is captable of showing a sustained train of action potentials and a biestable dynamical behaviour. Another important aspect of these works is to bring into consideration the temperature of the system as an additional parameter in the description of the squid axon electrical properties. Additionally, and from a mathematical point of view, the presence of Hopf bifurcations in the model means that the steady state solution must suffer a change in its local stability properties. This change is associated with the generation of the oscilatory solutions. But these results also raised the following question: Is it possible to generate oscilatory solutions to the H&H model without changing the local stability properties of the steady state solution? In other words, is it possible to generate degenarate Hopf bifurcations in the H&H model? Hassard et al. found that this kind of bifurcation is indeed present in the model but only if the temperature of the system and the sodium conductance are change in the appropiate way. They claimed that these changes are plaussible from a physiological point of view although they didn't give any evidance that their results had been found in a biological preparation.

Objective:

Locally, there is not way of establish the difference between the two kinds of Hopf bifurcations. So it is necessary to develop a global analysis (using numerical tools) to establish the difference.

Results:

The two main results are:

1) It was possible to show that under the conditions in which the H&H model has a subcritical Hopf bifurcation, the evolution of the membrane potential shows an histeresis phenomena.

2) Additionally, it was possible to show that when the model shows a degenerate Hopf bifurcation, the

steady state solution does not change its stability properties unless a very strong external perturbation is given to the system.

Comments:

In my opinion, GENESIS is an appropiate software to develop compartamental models to describe the electrical properties of excitable systems. Its graphical capabilities are, in my opinion, the most interesting aspect of the software. I think tha GENESIS is not an appropiate software to develop mathematical analysis of a dynamical system. I am used to write my own code to develop numerical analysis of a mathematical model. So learning the syntax of GENESIS, in which it is very difficult to see the equatios, was my main problem.

MARTIN HUBER,Graduate Student, Physiology, Phillips -University-Marburg, Germany

Course Project: Electical Coupling Between Endogenous Bursting Neurons in Small Networks.

The aim of the project was two construct an endogenous bursting neuron and to study electical coupling between such neurons connected together in small networks.

1) Single neuron:

Each neuron consists of a T-type calcium channel, a leak conductance as well as standard sodium and potassium conductances associated with action potentials. The T-type calcium channel was constructed using a model by Wang, Rinzel and Rogawsky (J.Neurophysiol. Vol 66 N0 3 1991). I simplified their T-type channel so that it could be implemented in GENESIS by using tabchannels. In simplifying I skipped the additional slow inactivation (d-) gate. Together with the leak conductance the "two channel" cell shows oscillations in membrane potential when adding a constant hyperpolarizing current (-8e-11 amps) to the model. The name of the implemented Ca-channel is TCa_WRR91. To add a spike mechanism to the cell I included the sodium and potassium conductances of the Traub`91 model (Na_hip_traub91 and Kdr_hip_traub91). I also adjusted the EREST_ACT to a somewhat more depolarized level. With this modifications it was possible to get endogenaous bursting bhaviour in the model cell. In addition the cells behaviour with respect to the low-threshold calcium channel seems to be realistically.

2) Coupling between neurons: After constructing the single cell I worked on a setup to study electrical coupling in a small network of such bursters. The project then was extended to contain three endogenous bursters which essentially behave exactly equal. The setup allows, however, to change interactively the maximum conductances of each of the three cells, so that the network can contain three different basic types of neurons: endogenous bursting, tonic only or just passive RC. In addition current can be injected into each of the calls interactively to change the behaviour of the cells. For

example a bursting cell might be converted into a tonically firing one by injecting depolarizing currents. To make the setup more flexible I then used toggle boxes which allow to connect or disconnect each cell in the network so that every combination of cells (alone,two or three coupled, chain or ring formation) is possible.

3) Results

I did need quite an amount of time to get the T-type current working under GENESIS, because the desciption in this above mentioned paper was somewhat cumbersome. Finally it worked and I got a bursting cell which exhibits different functional states in its behaviour. Concerning network properties and the behaviour of the burster when connected to each other I observed several different types of synchronized activity between the single components. The behaviour with respect to coupling seems not to be very intuitive because of the complicated channel kinetics (nonlinearities etc) of the cells (even the only have three channels). I did not observe antiphasic spiking when coupling two of them weakly (see John Rinzels article). It might be because I do not have very much spikes per burst (as John Rinzel suggested) and it might also be becuase I did not have the time to explore the whole coupling parameter space. So it might be interestinmg to do so in some future times.

4) Files

I am sorry everything I programmed is badly documented. The Wang,Rinzel,Rogawsky based T-type channel is found in the file "T_CELL.g" (which includes basically the bursting cell). The complete script I made for the screen setup for the small electrotonic network is found in "cop_osc1.g". This file

contains everything I put together in GENESIS code during the four weeks. Both files are found in "/home/martin/test".

MICHAEL IRIZARRY, Medical Resident, Neurology, Massachusetts General Hospital, MA *Course Project: Membrane Properties of a Neostriatal Neuron and Dopamine Modulation*

The purpose of my project was to model the membrane properties of the neostriatal neuron, in particular the anomalous rectification in the hyperpolarized and depolarized direction, and to model the effects of dopamine on these membrane properties. The simulation (using Neurokit) included two compartments, a soma with four channels and a dendrite with an excitatory glutaminergic synapse (userprefs.g and cell.p). The soma contained Hodgkin-Huxley Na and K channels (as in hhchan.g) as a spike generating mechanism after an supra-threshold current injection. A persistent sodium current, NaP, was constructed as a tabchannel (NaPchan.g) and provided membrane rectification in the depolarizing direction (a particular injection of current produced a larger voltage response than with merely the HH Na channel.)

A potassium inward rectifyer current, Kir, was also constructed as a tabchannel (Kirchan.g) and provided membrane rectification in the hyperpolarizing direction (a particular injection of current produced a smaller voltage response than with merely the HH K channel.) The effects of TTX could be modeled by decreasing the sodium conductances (both HH Na and NaP) by 90 %, resulting in a reduction in the membrane rectification in the depolarized (but not hyperpolarized) direction. The effects of TEA could be modeled by decreasing the potassium conductances (both HH K and Kir) by 90 % resulting in a reduction in the membrane rectification in the hyperpolarized direction. The neuromodulatory effects of dopamine were modelled by reducing the NaP current by 90 - 99 %. This resulted in a reduction of the membrane rectification in the depolarized direction. Furthermore, 0.2 nA current injections, which produced a series of action potentials in the control case, no longer generated an action potential; 0.3 nA current injection produced action potentials at a slower rate than in the control case; EPSP's evoked by the glutaminergic synapse were also of decreased amplitude (a perhaps of slightly less duration) than in the control case. Thus, by modelling the neuromodulatory effect of dopamine as a reduction of the NaP current responsible for the membrane rectification in the depolarized direction, the reduction of membrane excitability by dopamine was reproduced. Other currents that were constructed as tabchannels but not implemented in the model include a fast sodium channel (McCorchan92.g) and an Ih current (McCorchan.g).

RANU JUNG, Postdoctoral Fellow, Cardiology, Case Western Reserve University, OH *Course Project: Leech Heart half-oscillator*

In this project the Leech heart neuron half-ocillator was simulated. The heart tubes of the leech are controlled by interneurons that lie in the third and fourth ganglia. Within a ganglion the right and the left interneuron are connected by mutually inhibitory coonections. This pair forms a half-oscillator which when isolated from the rest of the system continues to show oscillatory behaviour. Each heart interneuron (HN) continues to fire tonically when decoupled from the contralateral HN.

To model the activity of the half-oscillator initially one HN was simulated. Seven currents have been experimentally shown to contribute to the firing pattern of the interneurons. Data for simulating the channels that pass these currents was obtained from the published experimental results. Some of the data was also obtained by personal contact with the investigator Dr. Ron Calabrese. Neurokit was used to simulate a single cell with the aforementioned seven channels. The accuracy of the simulation was checked by comparing the experimental results obtained using voltage clamp techniques with the results obtained by performing voltage clamp in simulation. The HN was found to show satisfactory responses and exhibited spontaneous continuous firing.

Two of the above simulated HN's were then connected to form the half-oscillator. Each of the HN's provides graded synaptic inhibtion to the contralateral HN. The post-synaptic inhibitory current is dependent on the calcium concentration in the presynaptic HN. The results demonstrate the capability of the half-oscillator to function as a mixed oscillatory system. The initialization of inhibition is caused by the inhibitory current which is dependent on the calcium concentration of the pre-synaptic HN (network property) while the termination of inhibition occurs because of an 'escape' from inhibition due to the

presence of the H - current (endogenous cellular propery).

While the model shows ocillations, they are currently not sustained. Hence, the parameter space for the simulation of the mutual inhibition needs to be further investigated. It is expected that this preliminary modeling will lead to further development of the complete central pattern generator of the Leech heart.

NOTE: The source of the experimental data is indicated within the program script. We now have a tabchannel2 which allows the Ca conc to be used to calculate an injection current. Although there are problems with the oscillator, the single heart neuron of the leech does work quite well. If anybody needs tabchannels for K,Ca, A current, and H current I have them in my files. The single cell simulation is under subdirectory "leechkit" in my home directory. It uses Neurokit for running the simulation. The half oscillator is under the subdirectory "lc_osc" under my home directory. It uses a MultiCell format.

BRANDT KEHOE, Faculty, Physics, California State University, Fresno, CA

Course Project: Interspike Interval Distributions Generated by Model Neurons

I In a 1954 paper, Gerstein and Mandelbrot (GM) developed a two parameter diffusion equation based model for the interspike interval (ISI) distribution function. The resulting distribution is:

$$P(t) = N(a,b)\ t^{(-3/2)}\ \exp[-a/t - bt]$$

where t is the ISI. In this model a depends upon the threshold level
and b depends upon the input rate. Their paper includes quite reasonable fits to a limited amount of experimental data. Examination of ISI data from Fuster's extracellular recordings from single cells in behaving monkeys suggests, with limitations discussed below, that the GM fit appears to characterize the data quite well, including good three parameter (a, b1, b2) fits to cells responding in two different input environments with quite different firing rates.

I propose developing a single neuron (a simple representation of a pyramidal neuron) with NEURON, with stochastic synaptic input; to explore the conditions necessary for output consistent with the GM model; and to get some insight into what characteristics of the neuron determine the GM parameters. If that is successful, I would like to employ existing, more sophistocated neuron models to extend the process, and, time permitting, begin to develop the same model on GENESIS so that I can carry out the same studies on models as they become available in babel.

****

A working program using j4defs.hoc in NEURON was successful, and run with the following characteristics: excitatory synaptic events occured with frequency specified, located randomly over the surface area of the dendritic membrane, randomly in time. All of those were alpha currents with Tpeak 1.5 msec and Gmax distributed randomly between 0.1 nS and 0.5 nS, with Erev = 0. Of those events, 80% included NMDA channels as implemented by synapse(). In addition, inhibitive events were distributed at a rate equal to 20% of the excitatory synaptic input rate, uniformly over the soma and dendrites out to the third branching. They had equal probability of being GABAa (t 10 msec, g 1 nS, E -70) and GABAb (t 40 msec, g 0.1 nS, E -95).

Soma properties:

```
psection()
soma { nseg=1  L=23.056
        /*location 0 attached to cell -1*/
        /* First segment only */
        insert morphology { diam=17.021}
        insert capacitance { cm=1}
        insert passive { g=5e-05 erev=-66}
insert info { fe_info=0.284226 fia_info=1 fib_info=0.0226696 flag_info=1} insert iap { gnabar_iap=0.2
```

gkbar_iap=0.12)
insert ical { gcabar_ical=0.0006)
insert ic { gkbar_ic=0.045 cai_ic=0)
insert ca_ion { eca=115 cai=0.001 cao=10) insert ia { gkbar_ia=0.001)
insert im { gkbar_im=0.0006)
insert k_ion { ek=-95 ki=0 ko=0)
insert inap { gnabar_inap=0.001)
insert na_ion { ena=50 nai=15.7 nao=116)
insert iar { gfastbar_iar=0.0008 gslowbar_iar=0.0002) insert armix_ion { earmix=-50 armixi=1 armixo=1}

Over an input rate for excitatory synapses between 13 kHz and 21 kHz the neuron fired at rates between 10 and 60 Hz. Runs were for 5000 msec each. The resulting isi distributions fit the GM form quite well except for the highest input rate where the GM distribution peaked at higher isi than the data. values of Cv rose from 0.31 at the lowest frequency, peaked at 0.38 with the input at 16 kHz (output at 26 Hz), and then declined to 0.28 at the highest frequency.

There was no opportunity to vary the parameters described above. I hope to continue this study to look at higher frequencies; to vary parameters of the input to the neuron and observe the effect on GM parameters a and b, and on Cv. The experimental (Fuster IT neurons) data and the GM model suggest that a should be input independent - which I do not observe. I would like to explore parameter space to see if such a realm exists.

I also ran the program with time varying input to see if I could explain experimentally higher Cv values on that basis. The recurrent network model which David Zipser and I have been exploring suggests that even with constant input to the network in which the observed neuron exists, migration between attractors can occur which can result in a spike train with a higher Cv but one which is not immediately distinguishable from one associated with a constant input rate. My model quite easily results in Cv's twice those observed with a single frequency.

ILAN LAMPL, Graduate Student, Neurobiology, Hebrew University, Israel
Course Project: Oscillatory Activity of Inferior Olive Neurons

As I wrote in the beginning of the course, the aim of the project was to create a model of inferior olive neurons, and to find if subthreshold oscillations of the membrane potential can synchronize synaptic inputs.

The model of the neurons was a simple cell including one compartment that has the HH conductances (fast sudium conductance and delayed rectifier pottasium conductance) and Low threshold calcium conductance that was taken from a model for thalamic neurons, but was modified by me to mimic the behavior that I know from the Olivary neurons. another conductance was muscarinic K current that was taken from the neurokit ("yamadachan"). all this conductances gave some of the important features of the behavior the olivary neurons that able them to generate damp subthreshold oscillations after releasing from hypoerpolaryztion current. Injection of sinusoidal current in the model and giving synaptic inputs at the same time in different phases showed the same behavior that is seen in the real neurons: in frequencies of 2 to 6 Hz the model neuron generate a clear responses in a particular phase (relative to the sine wave voltage) independent on the exact phases in witch the synaptic inputs were given.

The second step was to see what happened when the synaptic inputs arrive when there are damp oscillation without sine current injection. and the in the model the damp oscillations can also synchronize synaptic inputs. this type of behavior was not clearly expected so this is a real prediction. Coupling of two indentical cells by weak coupling while there are two synaptic inputs (one for each cell) that income in the upper stroke of the damp sub- threshold oscillations, in different times, increasing the synchronization between the responses of the cells. this is also a prediction and it is difficult yet to find out

if it also exist in the real neurons.

The second project that I did was to find how much time it take to a low threshold potential to propagate through a chain of cells that are coupled electrotonicly. The assumption were that large number of inferior olive cells are coupled in the nucleus. and the finding from the experiments that stimulation of the brain stem slice, extracellularily, any were in the nucleus, and recording from one of the cells, give response after 100-500 ms. my hypothesis was that this can be explained by the time of propagation of action potential (low threshold calcium spike) wave through the chain. The model shows that this could be the case, but I still have to show this experimentely.

MITCHELL MALTENFORT, Graduate Student, Biomedical Engineering, Northwestern University, Chicago, IL

Course Project: A Model Motoneuron and Renshaw Cell

Since I wasn't able to match a Genesis neuron model to specific behavior (rheobase, current-rate curves, etc), I instead took models from Traub (1977) for a model motoneuron and Renshaw cell (the latter based on some guesswork - to date, we know nada/zilch/bubkiss about Renshaw cell membrane) and wired up a very simple network. I had a tonic motoneuron, excited by a constant leakage channel; a phasic motoneuron, which received inputs from a "random" object; and a Renshaw cell, which was also excited by a constant leakage channel, for a ~12 Hz firing rate. The two motoneurones excited the Renshaw cell, which in turn inhibited the motoneurones.

There were three graphs: one for neuron outputs, one for the peristimulus time histogram (PSTH) of phasic motoneuron response to random input, and one for the interspike interval of the tonic motoneuron. My working hypothesis of Renshaw cell function is that it exists to foul up motoneuron firing synchrony. So I wanted to see what effects the two motoneruones would have on each other's firing, given the Renshaw-mediated interactions. As predicted from my work in Chicago, the tonic firing motoneuron was affected by even small synaptic inputs from the Renshaw cell: the PSTH went from a smooth delta function to a clump of spikes. I was initially surprised that the phasic firing was not terribly bothered by the Renshaw cell, but then it was firing irregularly and my hypothesis is that the Renshaw exists to prevent regularities.

USEFUL BITS

Not much new, although anybody playing with the interspike or peristim objects may want to get a look at how I set up the graphing. Also, the leakage channels have a funny definition - look at either "renshaw.g" or "moto.g". I set the creation of motoneurons and Renshaw cells up as functions in separate files because I like modularity; Dave Berkowitz (who helped me with the leakage channels) told me that that's not "proper" Genesis form, though.

FUTURE PLANS

Unfortunately, I came here with a certain amount of intellectual investment in a model that did not easily port to Genesis. So I will not use it. However, I'm shipping Genesis home for the benefit of a few people who may want to write objects for looking at muscle models.

FERENCE MECHLER, Graduate Student, Neural Science, New York University, New York City, NY

Course Project: Cortical Simple Cells in Area 17 of the Cat

The problem I chose to investigate is related to cortical simple cells in Area 17 of the cat. In in vivo experiments it has been demonstrated that

these cells change their response dynamics when temporally rich stimuli are applied instead single drifting sinousoidal gratings. The change in the response characteristics involves the change in the shape of the temporal frequency tuning curve and the shortening of the apparent integration time (C.Reid et al, J. Vis.Neurosci. 1992). It has been suggested that a change in the cells' time constant under stimulation with a combined stimuli of different temporal component sinusoids (the rich stimulus) may account, in part, for the shortening of the integration time, in consistency with the findings in the simulation of a cortica pyramidal

cell with realistic background activity, by O.Bernander et al.(PNAS, 1991)
I used Genesis for this simulation project. I planned to set a network of units to represent a patch of visual cortex. The number of units in this cortical network would be on the order of a thousand. There are three different celltypes in the model, following the canonical microcircuitry model of R.J.Douglas et al. (J.Physiology, 1991). Each unit is represented by a two-compartment, one for the dendritic processes, incorporating synaptic inputs and the other for the spike-generating soma that also receives synaptic inputs. Only four channels are used at current stage, 2 hh-type channels in the soma compartment, and a Na-channel for epsps and a K-channel for ipsps in the dendrite. Connectivity is mutual between cells, and all three types are connected to the others with synapse and all get synaptic input from the LGN. Two of the neuron types represent pyramidals, superficial (small) and deep layer (large) pyramidals, respectively. The third type is inhibitory interneuron.
Much of the time I spent on experimenting with the cell prototypes, varying parameters of conductances, synaptic weight, etc. in order to capture as much of the known physiological properties (R_in, Vm, synapse density, etc) as possible while keeping it simple for the rescaled model. This unfinished stage of the work can be seen in the subdirectory "cells" of my home directory, in e.g file threecells.g". I did not want to proceed to the large scale network before a firm understanding of the rescaling parameters. Planned, but not yet done, are: i) creation of lgn input to each unit; ii) weight function to describe synaptic weight vs distance between units; iii) output analysis making use of psths. The analysis of the problem described in the introduction would only come after this.

JILL NICOLAUS, Graduate Student, Organismal Biology and Anatomy, University of Chicago, IL *Course Project: Network Models of Inhibition in Turtle Visual Cortex*

My major goal for this course was to learn enough about the use and capabilities of GENESIS to utilize it in simulating networks of simplified neurons of several compartments. Although my actual project has not progressed beyond modifying the Neurokit simulation to produce an electrotonic model similar to that which I had previously created using Mathematica, I have become sufficiently familiar with GENESIS to extend my model as planned once I return to Chicago. That I did not finish a larger portion of my project during the course is due to my initial lack of familiarity with teh UNIX environment and to my decision to concentrate on learning from the many excellent lecturers and on experimenting with a number of different sorts of simulations, on the assumption that learning how to do a large number of things while I was here would be more valuable than completing sections of a fairly specific project. I expect to be relying on GENESIS as a tool for combining morphological and physiological experimental parameters into network models of inhibition in turtle visual cortex. Additionally, having just learned that the newest version of NEURON allows the construction of networks from single neuron models, I plan to spend some portion of my remaining time here learning something about NEURON so I can compare & possibly use both simulators.

MONICA PAOLINI, Graduate Student, Cognitive Science, University of California, San Diego, CA *Course Project: Poggio Model of the Optical Flow*

I kept on working on the Poggio model of the optical flow. The initial idea
was to write some C code to simulate MT either input or output and, the, to have a two layer network in Genesis simulating MT and MST. MT cells should have been selective for speed and direction and MST cells should have detected rotation and contraction/dilation independently of the location of the foe.
I finally ended up working in C, since I needed a too larger number of neurons to work on Genesis. Unfortunately though in C the project was much less interesting since the only thing I could do is to show that a mathematical model which has proven to work, indeed worked. In Genesis, it would have been much more interesting because I could have looked at the plausability of the model.

YIFAT PRUT, Graduate Student, Physiology, Hebrew University, Israel
Course Project: The Single Cell as a Coincidence Detector

and EYAL SEIDEMANN, Graduate Student, Biophysics, Tel Aviv University, Israel

Course project: Models of Attracter Neurons Networks Operating in Low Spike Rate

The motivation for the project was addressing the question of the single cell as a coincidence detector. To do so, we used a detailed model of a pyramidal cell (adapted from Ojvind work on NEURON), according to the data given by Martin & Douglas. The neuron had 164 compartments. We added active channels on the soma, using the Traub, tab-channels. All the rest of the cell was passive. Each compartment contained at least one synaptic input. The cell received two kind of inputs. The first one is a random uncorrelated synaptic input, this input was on each of the dendrits. The second type of the input was a synchronous input, which was send to a subset of the compartments. First we searched for the background parameters which will cause the cell to fire at about 1-2 Hz. Then, by changing the number of the synchronous synapses, and their efficacy, we tried to see to what extent the output cell preserve the structure of the synchronous input. By the end of the course, the simulation program was ready, and a several runs were made.
My further plans are to extend this simulation by decreasing the complexity of the single cell (up to a single compartment neuron), and the increase the number of the cell. By this it will be possible to investigate the property of a local network, which is composed by a coincident detector elements.

IRIS REUVENI, Graduate Student, Physiology, Ben Gurion University of the Negev, Israel *Course Project: The Role of Inhibition in Input Output Relation in Sparse Network*
The headline of the project is to see the role of inhibition in input output relation, in sparse network. the network contains 400 cells with simple mechanism. they include the spike generator and integrate synaptic inputs with alfa shape. 20% of the cells at the network are inhibitory neurons. every excitatory cell is connected to other 3 neurons. the threshold of each cell is 4 excitatory inputs. but the probability of each 2 neurons to be directly connected is less then 10%. the idea is to give set of input (group of cells that stimulus directly with DC current) measure the number of spikes that each neuron is firing at 100ms. to see the variance of the ressults dutring the time. and then to compare those results to the results obtain by implying other set of input. This kind of network kind reflect the initial condition of the system before it learned somthing. my aim to the future is to see how much the inhibition effect the dynamic of this network (how the varience is changing with time, or how much the inhibition alone can create atractors.), and how much it sensitive to the input.

EMILIO SALINAS, Graduate Student, Biophysics. National University, Mexico
Course Project: Simulation of the AB-PD Two-cell Network in the Stomatogastric Ganglion of the Lobster
My initial project concerned the simulation of the AB-PD two-cell network in the stomatogastric ganglion of the lobster (STG). Because neither of these two cells has a precise characterization in terms of channels and currents, the idea was (1) simulate the behavior of an LP neuron, whose currents are very well characterized and is also found in the STG pyloric rythm CPG, (2) modify its parameters so that it would resemble AB and PD cells, and (3) couple the AB-like and PD-like neurons.

The simulation of the LP cell involved eight different channels. Seven of those were included just as in the detailed model (Buchholtz, Golowasch and Marder, J. Neurophysiol vol 67 #2, Feb. 1992). I was not able to implement the last one, tha calcium activated potassium channel, because the differential equiation it obeys differs substantially from the form the tabchannels or other objects in GENESIS have. Instead of simply leaving out this last current, I put a Ca-K channel of the form used in the traub91chan.g script.

This "complete" version of the LP cell reproduced reasonably well a couple of graphs obtained with the Buchholtz et.al. original model. If it were possible to implement the original Ca-K channel, it would be quite straightforward to make a copy of this LP cell in order to have a two cell network, whose parameters could be varied so that it resembles the behavior of the AB-PD network.

At the moment I really don't have any specific future plans for the continuation of the project; if the idea were to take into account the morphological structure of the AB-PD dendritic tree, then it would be worthwhile to solve the Ca-K problem and continue using GENESIS; if not, then probably it would be much easier to use some ODE solver package that would allow any form for the differential equations of the

channel gates. In any case, GENESIS is an alternative that I will certainly keep in mind for future modelling, either for this same project of for another one.

I think there were a couple of new ideas developed while working with GENESIS. (1) the tabchannel object has 3 gates X, Y and Z, each of which obey the differential equation

$$dX/dt = (1 - beta(V))X - alpha(V)X$$

(or [Ca] instead of V in the case of Z), where alpha and beta (the steady state function along withthe time constant tau can also be used) have a specific functional form

$$alpha(x)= A + Bx / (C + exp((x+D)/F)$$

I modified this so that the alphas and betas could be expressed as

$$alpha(x) = A + Bx + G*exp((v+H)/I) / [C + E*exp((v+D)/F)]$$

which is a bit more general. The modified versions appear in /emilio/lp/lp_protodefs.g I think that having an even more general form for alpha and beta would be quite useful, because these are used only to fill in the tabulated values, so it would not slow down the simulation itself, just the setup. [Modified .simrc includes tableslib, with path to Maurice's sim/sources/tables directory.]

(2) It sometimes is quite useful to have the traditional X and Y gates being multiplied by a function of V or [Ca]. That could not be done with the tabchannel, because Z always obeyed a differential equation. I talked about this to Maurice, and we modified a couple of lines in the source code of the tabchannel in order to have a tabchannel2: an element that has traditional X and Y gates multiplied by a function Z = alpha(V) * beta(V), where V can really be whatever value is passed to Z through the CONCEN mesage.

My general comment on GENESIS is that it is not flexible enough when it comes to inserting a particular set of differential equations that describe the currents that flow thorugh the cell membrane. I do not know if this is caused by the numerical routines implemented (ODE solving methods) or just by the fact that it is asumed that most of the modelling is done with typical HH-like channels. In any case, my feeling is that if GENESIS were able to accept (easily) an arbitrary set of differential equations describing a particular current it would be much more powerful, at least with respect to the kinds of models I dealt with. (It already is a very neat simulator, I mean a very useful tool, but that does not mean it couldn't get even better!)

NANGIAVARAM SEKAR, Graduate Student, Neuroscience, University of Iowa, Iowa City *Couse Project: A Feedback Based Model of Synaptic Plasticity.*

The main objective of my project was to explore the plausibility of a feedback based model of Synaptic plasticity. Such models of synaptic plasticity have been implemented as connectionist models. This course has provided us the insight to have biophysical implementations of such connectionist models. Our model has been implemented using NEURON. The morphology of a layer 4 neuron was made available to us and our simulations were based on this neuron.

Synapses were distributed uniformly throughout the neuron. All synapses were excitatory and with the same distribution of NMDA and NON-NMDA synapses. The synapses were activated based on 2 different uniform distributions. To start with there was no temporal correlation between these 2 distributions. We intend to study the effect of different degrees of anti correlation between these distributions and their effects on the feedback. The feedback synapses' activation was calculated as a sigmoidal function of the average voltage of the soma,observed during the first 45 msec period. Such a feedback activation can be used to provide sufficient depolarization in the post synaptic neuron to activate the NMDA receptors and increase synaptic strength. The synaptic strength was decreased , if the synapses were activated without any post synaptic depolarization. We have had little success in altering the synaptic strength as a function of the calcium ion accumulation, that flows through the NMDA synapses and we intend to pursue this problem. This course has been helpful in

providing us the necessary tools to tackle the current problems in computational neuroscience.

MARK TOMMERDAHL, Faculty, Physiology, University of North Carolina, Chapel Hill, NC
Course Project: NMDA Receptor Effect on Neuron Responsivity at Low Velocities

In the S1 cortex, we have made extracellular recordings from pyramidal cells that show a range of velocity tuning curves. The upper layers of the cortex (layers 2 and 3) generally are tuned to the lower detectable velocities (1-5 cm/sec). The middle layer cells, on the other hand, are more sensitive to higher velocities (optimal tuning is between 10 and 20 cm/sec). Possibly correlated with this is a gradient of NMDA receptors (higher concentration in the upper layers). While there is certainly a network effect contributing to the response of the neurons, it would be interesting to see if the NMDA receptor could increase a neurons responsivity at low velocities. My project was to model a simple "idealized" neuron and measure the differential effect of sweeping a stimulus across the dendritic input at various rates (supposedly corresponding to different velocities) with and without the presence of NMDA receptors. My initial finding was that there is an increase in the responsivity of the neuron to lower velocity range with NMDA receptors present. The finding itself is no real surprise, as other (real) investigators have done much more exhaustive and detailed studies with similar results. Later, I strung a number of these neurons together, but had no real data (other than qualitative observations) to compare the results with. This turned out to be a good exercise in observing .

In general, although my project was relatively simple, I learned a great deal about compartmental modelling, and I found this to tie in very well with the lecture series. In particular, I plan on using the modelling approach, and this was an excellent opportunity to learn both the concepts and the actual mechanics of the process.

As far as the specifics of what-did-I-do for future users of GENESIS, I am afraid that I concentrated mainly on learning what was already available and simply made modifications to some of the tutorials (tutorial4, multicell, neurokit, orient) to fit my needs. I hope to set up a course within the next year that will utilize GENESIS for the lab section of the course.

YI-XIONG ZHOU, Graduate Student, Ophthalmology, McGill Vision Research Center, Canada
Course Project: Spatial Freqeuncy Properties of the Primary Visual Cortical Neurons

About What I Have Learned From This Course

One major benefit is the learning of using GENESIS to construct and analize neuronal networks. From the practice part of this course, I have learned to construct a simple network consisting single compartment neurons to simulate the spatial frequency tuning properties in the striate cortex neurons. Currently, this network is simple. However, it bears the potential to be easily modified into a much sophisticated circuit, which captures the biological features of the striate cortex circuits. Thus, this simple model designed in this course serves as a starting point to my future research developement. Two major questions are addressed in my future work: 1) to what extent the receptive field properties of the striate cortex neurons are contributed from the dLGN inputs, and 2) what is the intracortical connection contribution to the receptive field properties. The elegance of GENESIS is that it provides a way to analize the proposed questions quantitatively, by simply manipulating the connections between the LGN input and the cortical neurons, and the connections among cortical neurons. More importantly, the simulation is likely to reveal some dynamic properties of the cortical circuits which are critical for the responsive properties of the neurons, yet difficult to be observed by the traditional analytical method due to the complexity of the dynamics of the cortical circuits.

The lectures of this course exposed me to multiple active research areas regarding to the dynamical properties of the nervous system, ranging from microscopic/ionic-channel level to the macroscopic/behavior level. The contents of the lectures are stimulative. It is very difficult to describe this four-week intensive education in just several words. Anyway, I regard this course as an important step in

the developement of my research career.

Project Summary

In the practical part of the course, I modified the orientation tutorial script to simulate the spatial freqeuncy properties of the primary visual cortical neurons. A set of single compartment cortical neurons are created, which receive the dLGN neurons inputs. Two arrays of dLGN inputs are created. One is the on-cells and the other is the off cells. These cells are composed of a function generator whose output is feed into the rate field of a random spike generator. The connections from dLGN to cortical cells are by axon to the synapse. The size of the convergence from dLGN to cortex varies from neuron to neuron for allowing the cortical neurons having different preferred spatial frequencies. So far, there is no inter-connection among cortical neurons. This will be the next step of my work. Two versions of the simulation scripts have been written. One is used for genesis with graphcis and the other is for no graphics to speed up the simulation and to run under background. A modified version of GENESIS 1.4 is required, which is modified by Dieter who added a "new_peristim" object to do the stimulus histogram on the spike frequency. The major part of the simulation can be started by "xsf_all.g" under the genesis with graphics. To see the connections between dLGN and cortical neurons, click on the "xconn" button in the control window. Play arround, you can find the most information.